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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/837,344	04/19/2001	Claudine Guerin-Marchand	010830-116	2865

7590

02/10/2005

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EXAMINER

MINNIFIELD, NITA M

ART UNIT

PAPER NUMBER

1645

DATE MAILED: 02/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/837,344	GUERIN-MARCHAND ET AL	
	Examiner	Art Unit	
	N. M. Minnifield	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 November 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 31,32,35-37,39 and 40 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 31,32,35-37,39 and 40 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Response to Amendment

1. Applicants' amendment filed November 15, 2004 is acknowledged and has been entered. Claims 1-30, 33, 34 and 38 have been canceled. New claim 40 has been added. Claims 31, 32, 35-37, 39 and 40 are now pending in the present application. All rejections have been withdrawn in view of Applicants' amendment with the exception of those discussed below.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
3. Claims 36, 37 and now claim 40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are directed to a vaccine composition directed against malaria comprising a molecule having one or more peptide sequences bearing all or part of one or more T epitopes resulting from the infectious activity of *P. falciparum* in the hepatic cells. Claim 37 also recites that the T epitope is selected from the group of an amino acid sequence of SEQ ID NOS: 39-42, an amino acid sequence of SEQ ID NOS: 43-46 and amino acid sequence of SEQ ID NO. 19. SEQ ID NO: 41 is the selected species.

The specification at page 25 sets forth the Construction of Genomic DNA Library and page 26 sets forth Immunological Screening of Bank. The specification does not enable a vaccine composition directed against malaria comprising a molecule having one or more peptide sequences bearing all or part of one or more T epitopes resulting from the infectious activity of *P. falciparum* in the hepatic cells.

The state of the art indicates that at present there are no vaccines that protect against malaria. Kurtis et al 2001 states that a vaccine is urgently needed to stem the global resurgence of *P. falciparum* malaria; LSA-1 is one of a few proteins known to be expressed by liver-stage parasites, holds particular promise as a vaccine (abstract). Kurtis et al 2001 states that despite “important advances, such as the circumsporozoite protein (CSP)-based vaccine called RTS,S, the goal of a safe and broadly effective malaria vaccine remains unfulfilled. The parasite’s complex life-cycle offers several targets for intervention in the human host and the mosquito vector and vaccines against sporozoite, intrahepatic, blood and sexual stages of the parasite are currently in development.” (p. 219, col. 1). As of 2001, there is no effective vaccine that comprises the LSA either alone or in combination with other malaria proteins. Further, because LSA is a liver specific antigen, investigation of its immunological significance is restricted to human studies because no homologue in mouse or non-human primate malarias has been identified (p.219, col. 1). Others such as Taylor-Robinson et al 2001 have also indicated that LSA-1 may be a good candidate for a vaccine, but no vaccine has been produced that has been shown to be effective (see also Joshi et al 2000, Kurtis et al 1999, Cox, 1992). Shi et al, 1999 indicate that a multicomponent, multistage malaria vaccine can induce immune responses that inhibit parasite development at

multiple stages. The rationale and approach used in the development of a multicomponent *P. falciparum* vaccine will be useful in the development of a multispecies human malaria vaccine and vaccines against other infectious diseases (see abstract). “Although studies of immunogenicity and the results of *in vitro* protection experiments have been promising for many of the single stage-specific vaccine candidate antigens, the test of *in vivo* protection has not always been satisfactory. There is consensus, however, that a highly effective malaria vaccine would require a combination of key antigens and/or epitopes from different stages of the life cycle and that induction of both humoral and cellular immunity is required for optimal efficacy. Such a multicomponent malaria vaccine would also circumvent the problems associated with host genetic restriction and antigenic variability in the case of single antigen-based vaccines.” (Shi et al, 1999, p. 1615, paragraph bridging cols. 1-2). Shi et al 1999 also indicates that multiple protective immune responses against multiple antigens from different stages will be needed to protect against malaria (p. 1618, col. 2). “Although a single-antigen and/or stage-specific vaccine could provide protection against infections, there are several reasons to advocate a multivalent, multistage malaria vaccine. A major concern with a single antigen-based vaccine is that an antigenic variant population of the parasite not recognized by the vaccine will cause infection (with heterologous parasites) and cause disease.” (see p. 1618-1619).

In view of the fact that the specification does not set forth any enablement with regard to direction or guidance and the absence of working examples for the claimed vaccine composition, and the fact that the state of the art teaches that there are no single antigen or stage specific vaccines (i.e. LSA only) against malaria and the unpredictability and difficulty in obtaining an effective vaccine directed against

malaria comprising a molecule having one or more peptide sequences bearing all or part of one or more T epitopes resulting from the infectious activity of *P.*

falciparum in the hepatic cells there would be undue experimentation necessary for a person of skill in the art to practice the claimed invention.

Applicant's arguments filed November 15, 2004 have been fully considered but they are not persuasive. Applicants have asserted that simply because, as of 2001, no vaccines for malaria comprising LSA alone or in combination have been disclosed in the literature does not mean that LSA alone or in combination does not have vaccinating capabilities; and that it is well known in the art of malaria vaccines that vaccine clinical trials are extremely long-term studies that are carried out in many phases and that take more than ten to twelve years for the full set of clinical trials. However, it is noted that the claims are directed to a "vaccine composition against malaria", not a composition that has vaccinating capabilities. Further, it is not clear what Applicants mean by "vaccinating capabilities". The Examiner is aware of the long process (i.e. long terms studies, various phases in clinical trials) that is involved in the art of malaria vaccine, which points to the fact that there is no vaccine to protect against malaria.

Applicants have asserted that "even prior to the clinical trials, basic research must be conducted to identify potential useful antigens, vaccine concepts must be developed and evaluation of the antigen in animals is required. Finally, a manufacturing process for the clinical trial product must be created and evaluated. It will be appreciated that even to start a clinical trial extensive experiments and work must be undertaken, which takes many years. (See Appendix I)." A review of Appendix I points to the difficulties in malaria research. Page 2, col. 2 of

Appendix I asks the question, why is it so difficult to create a malaria vaccine. The reference states that parasites are much more complex than bacterial and viral organisms with 10-100 times more genetic information than simpler organisms. This reference appears to support the conclusions of the other references cited in the 112, first paragraph lack of enablement rejection. That being, that at the present time and in particular at the time of the filing date (1991) of the claimed invention, there were no malaria vaccines to protect against malaria; and that even ten years later, 2001, there is still no vaccine to protect against malaria. It is noted that the definition of a vaccine is a product that provides protection (prophylaxis) against infection, in this case protection against malaria. The pending specification does not set forth any enablement of a composition (vaccine or otherwise) that protects against malaria.

Pages 6 and 7 of the remarks discuss the differences between a humoral response and cellular immunity as well as T and B cell epitopes. Applicants have asserted that the specification does in fact describe B cell and T cell production with the antigens of the present invention. The Examiner appreciates these statements, however the claims are not directed to B cell and T cell production but rather to a vaccine composition directed against malaria. The enablement of the claimed invention is evaluated with regard to whether the specification sets forth a composition that protects a subject (animal or human) against malarial infection. Applicants have asserted that some of the documents cited by the Examiner indicate that the presently claimed invention is suitable for vaccines since immune responses were obtained. Again, the claims are not directed to a composition that is suitable for a vaccine, but actually to a vaccine that protects against malarial

infection. The generation of an immune response is not an indication of vaccine protection against malarial infection or any other type of infection.

Applicants have asserted that the mere fact that claims may encompass inoperative embodiments is not enough, by itself, to show lack of enablement. However, specific operative embodiments or examples of the invention must be set forth.

4. Claims 31, 35, 36 and 39 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 6319502. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the patent and pending application claim and/or disclose a polypeptide comprising at least one T epitope or B epitope from a liver-stage specific protein produce by *P. falciparum*, and compositions comprising the polypeptide.

This rejection is maintained for the reasons of record. It is noted that Applicants have requested that this rejection be held in abeyance until there is allowable subject; at that time Applicants will file a terminal disclaimer.

5. Claims 31, 35, 36 and 39 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 6270771. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the patent and pending application claim and/or disclose a polypeptide comprising at least one T epitope or B epitope from a liver-stage specific protein produce by *P. falciparum*, and compositions comprising the polypeptide.

This rejection is maintained for the reasons of record. It is noted that Applicants have requested that this rejection be held in abeyance until there is allowable subject; at that time Applicants will file a terminal disclaimer.

6. Claims 31, 32, 35-37, 39 and 40 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-16 and 25 of copending Application No. 09/900963. Although the conflicting claims are not identical, they are not patentably distinct from each other because both pending applications claim and/or disclose a polypeptide comprising at least one T epitope or B epitope from a liver-stage specific protein produce by *P. falciparum*, as well as vaccine compositions comprising a polypeptide comprising at least one T epitope or B epitope from a liver-stage specific protein produce by *P. falciparum*.

This rejection is maintained for the reasons of record. It is noted that Applicants have requested that this rejection be held in abeyance until there is allowable subject; at that time Applicants will file a terminal disclaimer.

7. No claims are allowed.

8. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.**

See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is 571-272-0860. The examiner can normally be reached on M-F (8:00-5:30) Second Friday Off.

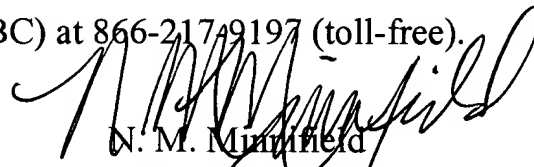
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette R.F. Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair->

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contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



N. M. Minnifield
Primary Examiner
Art Unit 1645

NMM
February 1, 2005